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FILE 'HOME' ENTERED AT 16:55:51 ON 20 AUG 2002

=> file medline caplus biosis

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:56:16 ON 20 AUG 2002

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FILE 'BIOSIS' ENTERED AT 16:56:16 ON 20 AUG 2002
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=> twik

L1          147 TWIK

=> potassium channel

L2        57435 POTASSIUM CHANNEL

=> inward? rectif?

L3        11769 INWARD? RECTIF?

=> l2 and l3

L4         6355 L2 AND L3

=> l4 and pore

L5          710 L4 AND PORE

=> l1 and l5

L6           20 L1 AND L5

=> l5 and (isolat? or purif?)

L7           79 L5 AND (ISOLAT? OR PURIF?)

=> l1 and (isolat? or purif?)

L8           31 L1 AND (ISOLAT? OR PURIF?)

=> l6 and (isolat? or purif?)

L9            4 L6 AND (ISOLAT? OR PURIF?)

=> l7 and 1970-1996/py

L10          12 L7 AND 1970-1996/PY
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=> dup rem l10

PROCESSING COMPLETED FOR L10
L11 6 DUP REM L10 (6 DUPLICATES REMOVED)

=> l8 and 1970-1996/py

L12 3 L8 AND 1970-1996/PY

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13 1 DUP REM L12 (2 DUPLICATES REMOVED)

=> l9 and 1970-1996/py

L14 3 L9 AND 1970-1996/PY

=> dup rem l14

PROCESSING COMPLETED FOR L14
L15 1 DUP REM L14 (2 DUPLICATES REMOVED)

=> l11 or l13 or l15

L16 6 L11 OR L13 OR L15

=> dup rem l16

PROCESSING COMPLETED FOR L16
L17 6 DUP REM L16 (0 DUPLICATES REMOVED)

=> d ti abs so l17 1-6

L17 ANSWER 1 OF 6 MEDLINE
TI **TWIK**-1, a ubiquitous human weakly **inward rectifying** K+ channel with a novel structure.
AB A new human weakly **inward rectifying** K+ channel, **TWIK**-1, has been **isolated**. This channel is 336 amino acids long and has four transmembrane domains. Unlike other mammalian K+ channels, it contains two **pore**-forming regions called P domains. Genes encoding structural homologues are present in the genome of Caenorhabditis elegans. **TWIK**-1 currents expressed in Xenopus oocytes are time-independent and present a nearly linear I-V relationship that saturated for depolarizations positive to O mV in the presence of internal Mg2+. This **inward rectification** is abolished in the absence of internal Mg2+. **TWIK**-1 has a unitary conductance of 34 pS and a kinetic behaviour that is dependent on the membrane potential. In the presence of internal Mg2+, the mean open times are 0.3 and 1.9 ms at -80 and +80 mV, respectively. The channel activity is up-regulated by activation of protein kinase C and down-regulated by internal acidification. Both types of regulation are indirect. **TWIK**-1 channel activity is blocked by Ba2+(IC50=100 microM), quinine (IC50=50 microM) and quinidine (IC50=95 microM). This channel is of particular interest because its mRNA is widely distributed in human tissues, and is particularly abundant in brain and heart. **TWIK**-1 channels are probably involved in the control of background K+ membrane conductances.

SO EMBO JOURNAL, **(1996 Mar 1)** 15 (5) 1004-11.
Journal code: 8208664. ISSN: 0261-4189.

L17 ANSWER 2 OF 6 MEDLINE
TI The human homologue of the weaver mouse gene in familial and sporadic Parkinson's disease.
AB The pathological hallmark of Parkinson's disease is cell death of dopaminergic neurons in the substantia nigra, resulting in striatal dopaminergic deficit and a clinical syndrome dominated by disorders of movement. The cause for this cell loss is unknown, but the possibility of a contributing genetic factor is increasingly recognized. Homozygous weaver mice, a mutant mouse strain, display progressive postnatal depletion of dopaminergic cells in the mesencephalon and have thus been proposed as an animal model for Parkinson's disease. Recently, mGIRK2, a putative G-protein **inward rectifier** K+ channel, has been identified as the causative gene in the weaver mouse and a homozygous mutation has been described in the H5 **pore** region of this channel. The human homologue of mGIRK2, KCNJ7 or hiGIRK2, has previously been **isolated** on chromosome 21q22.1. A possible involvement of this gene in the pathogenesis of Parkinson's disease has been discussed. To evaluate the possibility of a shared genetic defect in weaver mouse and Parkinson's disease, we analysed the H5 **pore** region of hiGIRK2 in familial and sporadic cases of Parkinson's disease. The sequence was normal in all cases examined, suggesting a differing aetiology of nigral cell loss in Parkinson's disease and weaver mice.
SO NEUROSCIENCE, **(1996 Jun)** 72 (4) 877-9.
Journal code: 7605074. ISSN: 0306-4522.

L17 ANSWER 3 OF 6 MEDLINE
TI Block of large conductance Ca(2+)-activated K+ channels in rabbit vascular myocytes by internal Mg2+ and Na+.
AB 1. We studied the biophysical properties of single large conductance (> 200 pS in symmetrical K+ pipette and bath solutions) Ca(2+)-activated K+ (BKca) channels of rabbit portal vein and coronary arterial smooth muscle cells using the cell-attached and inside-out variants of the patch-clamp technique (at 22 degrees C). 2. The unitary conductance of BKca channels recorded in cell-attached patches with K+ concentrations in the range 5.4-140 mM was significantly lower than that predicted on the basis of the conductance measured in inside-out patches with symmetrical K+ pipette and bath solutions (140 mM) and the constant field equation. In cell-attached patches from cells bathed in depolarizing medium (140 mM) with 5.4 mM K+ in the pipette solution, BKca channels were difficult to detect on the physiological range of membrane potentials (approximately -50 mV). Unitary currents were smaller at all voltages in the range -50 to 0 mV and the i-V relationship exhibited strong **inward rectification** at potentials > 0 mV. These channels were unequivocally identified as BKca channels due to their sensitivity to caffeine (10 mM) and iberiotoxin (20 nM), and their non-stationary kinetic properties. 3. Exposure of the cytoplasmic side of excised patches to [Mg2+] in the range 0-15 mM produced two effects on BKca channel activity: the slope conductance and open probability were reduced and enhanced, respectively, in a concentration-dependent manner by this cation. The Mg(2+)-induced reduction in conductance exhibited weak voltage dependence. 4. Application

of 20 mM Na+ to the internal face of BKca channels recorded in the inside-out configuration produced a flickery block at potentials > or = +20 mV resulting in reduced unitary current amplitudes and strong **inward rectification** of the i-V relationship. Exposure of inside-out patches to a combination of 20 mM Na+ and 2 mM Mg2+ further reduced unitary current amplitude to a level similar to the algebraic sum of the effect of each cation in **isolation**. 5. We conclude that Ca(2+)-dependent K+ channels of vascular smooth muscle cells display a lower unitary conductance when recorded under physiological conditions than that previously estimated on the basis of their behaviour in excised membrane patches. Our data indicate that the decreased permeation through BKca channels may be partly attributed to block by intracellular Mg2+ and Na+, which appear to interact with distinct binding sites along the inner side of the **pore**.

SO JOURNAL OF PHYSIOLOGY, **(1996 Sep 15)** 495 (Pt 3) 701-16.
Journal code: 0266262. ISSN: 0022-3751.

L17 ANSWER 4 OF 6 MEDLINE

TI Molecular dynamics simulations of **isolated** transmembrane helices of **potassium channels**.

AB In the middle of the S6 helix in voltage-gated **potassium channels** there is a highly conserved Pro-Val-Pro motif, while the equivalent M2 helix of **inward rectifier potassium channels** contains a conserved glycine residue in a comparable position. The structural implications of these conserved motifs are of interest given the evidence that S6 and M2 are components of the lining of their respective **pores**. Multiple sequence alignment and TM helix prediction methods were used to define consensus regions for S6 and M2. Ensembles of 50 structures for each helix were generated by simulated annealing and restrained molecular dynamics. Time-dependent fluctuations of S6 and M2 were investigated by long time scale molecular dynamics simulations on representative members of each ensemble carried out in vacuo in the presence and absence of a hydrophobic potential that mimics a lipid bilayer. The results are discussed in terms of the structural basis of the kink in S6 and M2 and of a putative functional role for flexible helices as "molecular swivels."

SO BIOPOLYMERS, **(1996 Oct)** 39 (4) 503-15.
Journal code: 0372525. ISSN: 0006-3525.

L17 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS

TI A new family of outwardly rectifying **potassium channel** proteins with two **pore** domains in tandem

AB **Potassium channels** catalyze the permeation of K+ ions across cellular membranes and are identified by a common structural motif, a highly conserved signature sequence of 8 amino acids in the P domain of each channel's **pore**-forming .alpha.-subunit. A novel K+ channel (TOK1) was **isolated** from Saccharomyces cerevisiae that contains two P domains within one continuous polypeptide. Xenopus laevis oocytes expressing the channel exhibit a unique, outwardly rectifying, K+-selective current. The channel is permeable to outward flow of ions at membrane potentials above the K+ equil. potential; its conduction-voltage relationship is thus sensitive to extracellular K+ ion concn. In excised membrane patches, external divalent cations block the channel in a voltage-dependent manner, and their removal in this configuration allows inward channel current. These attributes are similar to those described for **inwardly rectifying** K+ channels, but in the

opposite direction, a previously unrecognized channel behavior. The results identify a new class of K+ channel which is distinctive in both its primary structure and functional properties. Structural homologs of the channel are present in the genome of Caenorhabditis elegans.
SO Nature (London) (**1995**), 376(6542), 690-5
CODEN: NATUAS; ISSN: 0028-0836

L17 ANSWER 6 OF 6 MEDLINE
TI Cloning a novel human brain **inward rectifier potassium channel** and its functional expression in Xenopus oocytes.
AB We have cloned a novel **inward rectifier** K+ channel (hIRK2) from a human frontal cortex cDNA library. The amino acid sequence of hIRK2 shares 60% and 40% identity with the mouse IRK1 and the rat ROMK1 channels, respectively. Xenopus oocytes injected with hIRK2 cRNA showed an **inwardly rectifying** K+ current that had a prominent 'N-shape' I-V curve and was blocked by extracellular Ba2+. The hIRK2 channel has two unique features: (a) an 18 amino acid insertion between the first transmembrane region and the **pore**, and (b) restricted mRNA distribution found only in human brain and heart.
SO FEBS LETTERS, **(1994 Jul 18)** 348 (3) 239-43.
Journal code: 0155157. ISSN: 0014-5793.

=> lesage?/au

L18 2097 LESAGE?/AU

=> florian?/au

L19 2011 FLORIAN?/AU

=> l18 and l19

L20 0 L18 AND L19

=> guillemare?/au

L21 70 GUILLEMARE?/AU

=> eric?/au

L22 25421 ERIC?/AU

=> l20 and l21

L23 0 L20 AND L21

=> fink?/au

L24 40590 FINK?/AU

=> michel?/au

L25 49136 MICHEL?/AU

=> l23 and l24

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L26           0 L23 AND L24

=> lazdunski?/au

L27        2486 LAZDUNSKI?/AU

=> l25 and l27

L28          20 L25 AND L27

=> l17 and l28

L29           0 L17 AND L28

=> romey?/au

L30         680 ROMEY?/AU

=> georges?/au

L31        7034 GEORGES?/AU

=> l30 and l31

L32           0 L30 AND L31

=> barhanin?/au

L33         367 BARHANIN?/AU

=> jaques?/au

L34        1569 JAQUES?/AU

=> l33 and l34

L35           0 L33 AND L34

=> d his


     (FILE 'HOME' ENTERED AT 16:55:51 ON 20 AUG 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 16:56:16 ON 20 AUG 2002
L1          147 TWIK
L2        57435 POTASSIUM CHANNEL
L3        11769 INWARD? RECTIF?
L4         6355 L2 AND L3
L5          710 L4 AND PORE
L6           20 L1 AND L5
L7           79 L5 AND (ISOLAT? OR PURIF?)
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L9            4 L6 AND (ISOLAT? OR PURIF?)
L10          12 L7 AND 1970-1996/PY
L11           6 DUP REM L10 (6 DUPLICATES REMOVED)
L12           3 L8 AND 1970-1996/PY
L13           1 DUP REM L12 (2 DUPLICATES REMOVED)
L14           3 L9 AND 1970-1996/PY
L15           1 DUP REM L14 (2 DUPLICATES REMOVED)
L16           6 L11 OR L13 OR L15
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L17             6 DUP REM L16 (0 DUPLICATES REMOVED)
L18          2097 LESAGE?/AU
L19          2011 FLORIAN?/AU
L20             0 L18 AND L19
L21            70 GUILLEMARE?/AU
L22         25421 ERIC?/AU
L23             0 L20 AND L21
L24         40590 FINK?/AU
L25         49136 MICHEL?/AU
L26             0 L23 AND L24
L27          2486 LAZDUNSKI?/AU
L28            20 L25 AND L27
L29             0 L17 AND L28
L30           680 ROMEY?/AU
L31          7034 GEORGES?/AU
L32             0 L30 AND L31
L33           367 BARHANIN?/AU
L34          1569 JAQUES?/AU
L35             0 L33 AND L34

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